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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Applicant:** Nancy A. Noble et al.  
**Serial No.:** 09/869,820  
**Filed:** July 5, 2001  
**Docket:** 30434.4USWO  
**Title:** METHODS FOR TREATING CONDITIONS ASSOCIATED WITH THE ACCUMULATION OF EXCESS EXTRACELLULAR MATRIX

CERTIFICATE UNDER 37 CFR 1.8

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By: Renato Marco P. Domingo  
Name: Renato Marco P. Domingo

Assistant Commissioner for Patents  
Washington, D.C. 20231

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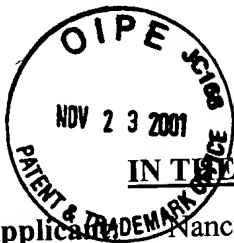
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**MANDEL & ADRIANO**  
35 No. Arroyo Parkway, Suite 60  
Pasadena, California 91103  
(626) 395-7801

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Examiner: Not yet known

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Group Art Unit: 1642

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By: Renato Marco P. Domingo

INFORMATION DISCLOSURE STATEMENT (37 C.F.R. § 1.97(b)(3))Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- U.S. Patent No. 5,571,714 issued November 5, 1996 – **Exhibit 1**
- International Publication No. WO91/04748 published April 18, 1991 – **Exhibit 2**
- International Publication No. WO93/09800 published May 27, 1993 – **Exhibit 3**
- International Publication No. WO93/10808 published June 10, 1993 – **Exhibit 4**
- International Publication No. WO96/25178 published August 22, 1996 – **Exhibit 5**
- International Publication No. WO97/39028 published October 23, 1997 – **Exhibit 6**
- International Publication No. WO99/34823 published July 15, 1999 – **Exhibit 7**
- Abboud, Hanna E., "Platelet-derived growth factor and mesangial cells," *Kidney International*, 41:581-3, 1992 – **Exhibit 8**

- Anderson, Sharon et al., "Control of Glomerular Hypertension Limits Glomerular Injury in Rats with Reduced Renal Mass," *The Journal of Clinical Investigation*, 76:612-9, 1985 – **Exhibit 9**
- Antonipillai, I. et al., "Transforming growth factor- $\beta$  is a renin secretagogue at picomolar concentrations," *American Journal of Physiology*, 265:F537-41, 1993 – **Exhibit 10**
- Arai, N. et al., "Complete Nucleotide Sequence of the Chromosomal Gene for Human IL-4 and Its Expression," *Journal of Immunology*, 142:274-82, 1989 – **Exhibit 11**
- Arai, Makoto et al., "In Vivo Transfection of Genes for Renin and Angiotensinogen into the Glomerular Cells Induced Phenotypic Change of the Mesangial Cells and Glomerular Sclerosis," *Biochemical and Biophysical Research Communications*, 206:525-32, 1995 – **Exhibit 12**
- Armelin, Hugo A., "Pituitary Extracts and Steroid Hormones in the Control of 3T3 Cell Growth (mouse fibroblasts/growth factor)," *Proceedings of the National Academy of Sciences USA*, 70:2702-6, 1973 – **Exhibit 13**
- Arnheim, Norman and Henry Erlich, "Polymerase Chain Reaction Strategy," *Annual Review of Biochemistry*, 61:131-56, 1992 – **Exhibit 14**
- Badasso, M. et al., "Crystallization and Preliminary X-ray Analysis of Complexes of Peptide Inhibitors with Human Recombinant and Mouse Submandibular Renins," *Journal of Molecular Biology*, 223:447-53, 1992 – **Exhibit 15**
- Bagchus, W. M. et al., "Glomerulonephritis Induced by Monoclonal Anti-Thy 1.1 Antibodies," *Laboratory Investigation*, 55:680-7, 1986 – **Exhibit 16**
- Baricos, William H. et al., "ECM degradation by cultured human mesangial cells is mediated by a PA/plasmin/MMP-2 cascade," *Kidney International*, 47:1039-47, 1995 – **Exhibit 17**
- Baricos, William H. et al. "Transforming Growth Factor- $\beta$  is a Potent Inhibitor of Extracellular Matrix Degradation by Cultured Human Mesangial Cells," *Journal of the American Society of Nephrology*, 10:790-5, 1999 – **Exhibit 18**

- Beaucage, S. L. and M. H. Caruthers, "Deoxynucleoside Phosphoramidites – A New Class of Key Intermediates for Deoxypolynucleotide Synthesis," *Tetrahedron Letters*, 22:1859-62, 1981 – **Exhibit 19**
- Bennett, C. Frank et al., "Cationic Lipids Enhance Cellular Uptake and Activity of Phosphorothioate Antisense Oligonucleotides," *Molecular Pharmacology*, 41:1023-33, 1992 – **Exhibit 20**
- Bongartz, Jean-Pierre et al., "Improved biological activity of antisense oligonucleotides conjugated to a fusogenic peptide," *Nucleic Acids Research*, 22:4681-8, 1994 – **Exhibit 21**
- Border, Wayne A. and Nancy A. Noble, "Transforming Growth Factor  $\beta$  in Tissue Fibrosis," *New England Journal of Medicine*, 331:1286-92, 1994 – **Exhibit 22**
- Border, Wayne A. and Nancy A. Noble, "TGF- $\beta$  in kidney fibrosis: A target for gene therapy," *Kidney International*, 51:1388-96, 1997 – **Exhibit 23**
- Border, Wayne A. and Nancy A. Noble, "TGF- $\beta$ ," *Scientific American Science & Medicine*, 2:68-77, 1995 – **Exhibit 24**
- Border, Wayne A. and Nancy A. Noble, "Evidence that TGF- $\beta$  should be a therapeutic target in diabetic nephropathy," *Kidney International*, 54:1390-1, 1998 – **Exhibit 25**
- Border, Wayne A. and Nancy A. Noble, "Interactions of Transforming Growth Factor- $\beta$  and Angiotensin II in Renal Fibrosis," *Hypertension*, 31:181-8, 1998 – **Exhibit 26**
- Border, Wayne A. and Erkki Ruoslahti, "Transforming Growth Factor- $\beta$  in Disease: The Dark Side of Tissue Repair," *Journal of Clinical Investigation*, 90:1-7, 1992 – **Exhibit 27**
- Border, Wayne A. et al. "Suppression of experimental glomerulonephritis by antiserum against transforming growth factor  $\beta$ 1," *Nature*, 346:371-4, 1990 – **Exhibit 28**
- Border, Wayne A. et al., "Natural inhibitor of transforming growth factor- $\beta$  protects against scarring in experimental kidney disease," *Nature*, 360:361-4, 1992 – **Exhibit 29**
- Border, Wayne A. et al., "Transforming growth factor- $\beta$  regulates production of proteoglycans by mesangial cells," *Kidney International*, 37:689-95, 1990 – **Exhibit 30**
- Boshart, Michael et al., "A Very Strong Enhancer is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus," *Cell*, 41:521-30, 1985 – **Exhibit 31**

- Boutorine, A. S. and E. V. Kostina, "Reversible covalent attachment of cholesterol to oligodeoxyribonucleotides for studies of the mechanisms of their penetration into eucaryotic cells," *Biochimie*, 75:35-41, 1993 – **Exhibit 32**
- Campbell, Duncan J. and Anthony J. Valentijn, "Identification of vascular renin-binding proteins by chemical cross-linking: inhibition of binding of renin by renin inhibitors," *Journal of Hypertension*, 12:879-90, 1994 – **Exhibit 33**
- Capaccioli, Sergio et al., "Cationic Lipids Improve Antisense Oligonucleotide Uptake and Prevent Degradation in Cultured Cells and in Human Serum," *Biochemical and Biophysical Research Communications*, 197:818-25, 1993 – **Exhibit 34**
- Chakraborty, Asit K. et al., "Synthetic retrotransposon vectors for gene therapy," *FASEB Journal*, 7:971-7, 1993 – **Exhibit 35**
- Chansel, Dominique et al., "Identification and regulation of renin in human cultured mesangial cells," *American Journal of Physiology*, 252:F32-8, 1987 – **Exhibit 36**
- Ciccarone, Valentina C. et al., "Identification of Enhancer-like Elements in Human IFN- $\gamma$  Genomic DNA," *Journal of Immunology*, 144:725-30, 1990 – **Exhibit 37**
- Coffin, in Weiss et al. (Eds.), *RNA Tumor Viruses*, 2nd Ed., Vol. 2, Cold Spring Laboratory, NY, pp. 17-73, 1985 – **Exhibit 38**
- Cole, S. P. C. et al., "The EBV-Hybridoma Technique and Its Application to Human Lung Cancer," *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc. 77-96, 1985 – **Exhibit 39**
- Compagnon, B. et al., "Targeting of Poly(rI)-Poly(rC) by Fusogenic (F Protein) Immunoliposomes," *Experimental Cell Research*, 200:333-8, 1992 – **Exhibit 40**
- Cook, R. Frank et al., "Retrotransposon Gene Engineering," *Biotechnology*, 9:748-51, 1991 – **Exhibit 41**
- Cote, Richard J. et al., "Generation of human monoclonal antibodies reactive with cellular antigens," *Proceedings of the National Academy of Sciences USA*, 80:2026-30, 1983 – **Exhibit 42**

- DePamphilis, M. L. et al., "Microinjecting DNA into Mouse Ova to Study DNA Replication and Gene Expression and to Produce Transgenic Animals," *BioTechniques*, 6:662-80, 1988 – **Exhibit 43**
- Dhanaraj, V. et al., "X-ray analyses of peptide-inhibitor complexes define the structural basis of specificity for human and mouse renins," *Nature*, 357:466-72, 1992 – **Exhibit 44**
- Dostal, David E. et al., "An Improved Method for Absolute Quantification of mRNA Using Multiplex Polymerase Chain Reaction: Determination of Renin and Angiotensinogen mRNA Levels in Various Tissues," *Analytical Biochemistry*, 223:239-50, 1994 – **Exhibit 45**
- Dzau, Victor J. and Jeffrey Kreisberg, "Cultured Glomerular Mesangial Cells Contain Renin: Influence of Calcium and Isoproterenol," *Journal of Cardiovascular Pharmacology*, 8:S6-10, 1986 – **Exhibit 46**
- Eltayeb, B. O. et al., "Effects of captopril on serum levels of TGF- $\beta$  in insulin-dependent diabetic patients," *Journal of the American Society of Nephrology*, 8:A0524, 1997 – **Exhibit 47**
- Felgner, Philip L. et al., "Lipofection: A highly efficient, lipid-mediated DNA-transfection procedure," *Proceeding of the National Academy of Sciences USA*, 84:7413-7, 1987 – **Exhibit 48**
- Felgner, P. L. et al., "Cationic Liposome Mediated Transfection," *Proceedings of the Western Pharmacology Society*, 32:115-21, 1989 – **Exhibit 49**
- Felgner, P. L. and G. Rhodes, "Gene therapeutics," *Nature*, 349:351-2, 1991 – **Exhibit 50**
- Fischli, Walter et al., "Ro 42-5892 is a Potent Orally Active Renin Inhibitor in Primates," *Hypertension*, 18:22-31, 1991 – **Exhibit 51**
- Flaumenhaft, Robert et al., "Activation of Latent Transforming Growth Factor  $\beta$ ," *Advances in Pharmacology*, 24:51-76, 1993 – **Exhibit 52**
- Fujita, Takashi et al., "Regulation of Human Interleukin-2 Gene: Functional DNA Sequences in the 5' Flanking Region for the Gene Expression in Activated T Lymphocytes," *Cell*, 46:401-7, 1986 – **Exhibit 53**

- Gibbons, Gary H. et al., "Vascular Smooth Muscle Cell Hypertrophy vs. Hyperplasia," *Journal of Clinical Investigation*, 90:456-61, 1992 – **Exhibit 54**
- Grainger, David J. et al., "The serum concentration of active transforming growth factor- $\beta$  is severely depressed in advanced atherosclerosis," *Nature Medicine*, 1:74-9, 1995 – **Exhibit 55**
- Greene, E. L. et al., "Role of Aldosterone in the Remnant Kidney Model in the Rat," *Journal of Clinical Investigation*, 98:1063-8, 1996 – **Exhibit 56**
- Gupta, Prem et al., "Transforming Growth Factor- $\beta$ 1 Inhibits Aldosterone and Stimulates Adrenal Renin in Cultured Bovine Zona Glomerulosa Cells," *Endocrinology*, 131:631-6, 1992 – **Exhibit 57**
- Haensler, Jean and Francis C. Szoka, Jr., "Polyamidoamine Cascade Polymers Mediate Efficient Transfection of Cells in Culture," *Bioconjugate Chem*, 4:372-9, 1993 – **Exhibit 58**
- Haraguchi, Masashi et al., "Recombinant Tissue Type Plasminogen Activator (rt-PA) Promotes Glomerular Plasmin Generation and Extracellular Matrix (ECM) Turnover in Anti-Thy-1 Nephritis," *Journal of the American Society of Nephrology*, 9:A2639, 1998 – **Exhibit 59**
- Horikoshi, Satoshi et al., "Water Deprivation Stimulates Transforming Growth Factor- $\beta$ 2 Accumulation in the Juxtaglomerular Apparatus of Mouse Kidney," *Journal of Clinical Investigation*, 88:2117-22, 1991 – **Exhibit 60**
- Huse, William D. et al., "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda," *Science*, 246:1275-81, 1989 – **Exhibit 61**
- Husted, Russell F. et al., "Induction of resistance to mineralocorticoid hormone in cultured inner medullary collecting duct cells by TGF- $\beta$ 1," *American Journal of Physiology*, 267:F767-75, 1994 – **Exhibit 62**
- Huxley, Clare, "Mammalian artificial chromosomes: a new tool for gene therapy," *Gene Therapy*, 1:7-12, 1994 – **Exhibit 63**
- Huxley, Clare et al., "Ordering Up Big MACs," *BioTechnology*, 12:586-90, 1994 – **Exhibit 64**

- Isaka, Yoshitaka et al., "Gene therapy by skeletal muscle expression of decorin prevents fibrotic disease in rat kidney," *Nature Medicine*, 2:418-23, 1996 – **Exhibit 65**
- Isaka, Yoshitaka et al., "Glomerulosclerosis Induced by In Vivo Transfection of Transforming Growth Factor- $\beta$  or Platelet-derived Growth Factor Gene into the Rat Kidney," *Journal of Clinical Investigation*, 92:2597-601, 1993 – **Exhibit 66**
- Isaka, Y. et al., "Decorin Gene Therapy for Experimental Glomerulonephritis," *Journal of the American Society of Nephrology*, 6:1261, 1995 – **Exhibit 67**
- Isaka, Yoshitaka et al., "Gene therapy by transforming growth factor- $\beta$  receptor-IgG Fc chimera suppressed extracellular matrix accumulation in experimental glomerulonephritis," *Kidney International*, 55:465-75, 1999 – **Exhibit 68**
- Johnson, Richard J. et al., "The Activated Mesangial Cell: A Glomerular "Myofibroblast"?", *Journal of the American Society of Nephrology*, 2:S190-7, 1992 – **Exhibit 69**
- Kagami, Shoji et al., "Angiotensin II Stimulates Extracellular Matrix Protein Synthesis through Induction of Transforming Growth Factor- $\beta$  Expression in Rat Glomerular Mesangial Cells," *Journal of Clinical Investigation*, 93:2431-7, 1994 – **Exhibit 70**
- Kagami, Shoji et al., "Coordinated Expression of  $\beta 1$  Integrins and Transforming Growth Factor- $\beta$ -Induced Matrix Proteins in Glomerulonephritis," *Laboratory Investigation*, 69:68-76, 1993 – **Exhibit 71**
- Kanai, Hidetoshi et al., "Angiotensin II upregulates the expression of TGF- $\beta$  type I and type II receptors," *Journal of the American Society of Nephrology*, 8:A2410, 1997 – **Exhibit 72**
- Karlsson, Stefan et al., "Transfer of genes into hematopoietic cells using recombinant DNA viruses," *Proceeding of the National Academy of Sciences USA*, 82:158-62, 1985 – **Exhibit 73**
- Karlsson, Stefan et al., "Stable gene transfer and tissue-specific expression of a human globin gene using adenoviral vectors," *EMBO Journal*, 5:2377-85, 1986 – **Exhibit 74**
- Kashgarian, Michael and R. Bernd Sterzel, "The pathobiology of the mesangium," *Kidney International*, 41:524-9, 1992 – **Exhibit 75**



- Kim, Seong-Jin et al., "Post-transcriptional Regulation of the Human Transforming Growth Factor- $\beta$ 1 Gene," *Journal of Biological Chemistry*, 267:13702-7, 1992 – **Exhibit 76**
- Kirschmeier, Paul T. et al., "Construction and Characterization of a Retroviral Vector Demonstrating Efficient Expression of Cloned cDNA Sequences," *DNA*, 7:219-25, 1988 – **Exhibit 77**
- Kitamura, Masanori et al., "Transfer of a mutated gene encoding active transforming growth factor- $\beta$ 1 suppresses mitogenesis and IL-1 response in the glomerulus," *Kidney International*, 48:1747-57, 1995 – **Exhibit 78**
- Klahr, Saulo et al., "The Progression of Renal Disease," *New England Journal of Medicine*, 318:1657-66, 1988 – **Exhibit 79**
- Köhler, G. and C. Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," *Nature*, 256:495-7, 1975 – **Exhibit 80**
- Kozbor, Danuta and John C. Roder, "The production of monoclonal antibodies from human lymphocytes," *Immunology Today*, 4:72-79, 1983 – **Exhibit 81**
- Kulkarni, Ashok B. et al., "Transforming growth factor  $\beta$ 1 null mutation in mice causes excessive inflammatory response and early death," *Proceedings of the National Academy of Sciences USA*, 90:770-4, 1993 – **Exhibit 82**
- Lawrence, Daniel A. et al., "Structure-Function Studies of the SERPIN Plasminogen Activator Inhibitor Type 1," *Journal of Biological Chemistry*, 265:20293-301, 1990 – **Exhibit 83**
- Lawrence, Daniel A. et al., "Localization of Vitronectin Binding Domain in Plasminogen Activator Inhibitor-1," *Journal of Biological Chemistry*, 269:15223-8, 1994 – **Exhibit 84**
- Lawrence, Daniel A. et al., "Characterization of the Binding of Different Conformational Forms of Plasminogen Activator Inhibitor-1 to Vitronectin," *Journal of Biological Chemistry*, 272:7676-80, 1997 – **Exhibit 85**
- Lawrence, Daniel A., "The Role of Reactive-Center Loop Mobility in the Serpin Inhibitory Mechanism," *Advances in Experimental Medicine and Biology*, 425:99-108, 1997 – **Exhibit 86**

- Leonetti, Jean-Paul et al., "Biological Activity of Oligonucleotide-Poly(L-lysine) Conjugates: Mechanism of Cell Uptake," *Bioconjugate Chem.*, 1:149-53, 1990 – **Exhibit 87**
- Leonetti, Jean-Paul et al., "Antibody-targeted liposomes containing oligodeoxyribonucleotides complementary to viral RNA selectively inhibit viral replication," *Proceedings of the National Academy of Sciences*, 87:2448-51, 1990 – **Exhibit 88**
- Letterio, John J. et al., "Maternal Rescue of Transforming Growth Factor- $\beta$ 1 Null Mice," *Science*, 264:1936-8, 1994 – **Exhibit 89**
- Linsley, Peter S. et al., "T-cell antigen CD28 mediates adhesion with B cells by interacting with activation antigen B7/BB-1," *Proceedings of the National Academy of Sciences USA*, 87:5031-5, 1990 – **Exhibit 90**
- Lopez-Armada, M. J. et al., "Immune Complexes Stimulate the Expression and Synthesis of Matrix Proteins in Cultured Rat and Human Mesangial Cells Role of Transforming Growth Factor  $\beta$ ," *Journal of the American Society of Nephrology*, 5:67P, 1994 – **Exhibit 91**
- Mann, Richard et al., "Construction of a Retrovirus Packaging Mutant and Its Use to Produce Helper-Free Defective Retrovirus," *Cell*, 33:153-9, 1983 – **Exhibit 92**
- Markowitz, Sanford et al., "Inactivation of the Type II TGF- $\beta$  Receptor in Colon Cancer Cells with Microsatellite Instability," *Science*, 268:1336-8, 1995 – **Exhibit 93**
- Marshall, Bruce C. et al., "Alveolar Epithelial Cell Plasminogen Activator," *Journal of Biological Chemistry*, 265:8198-204, 1990 – **Exhibit 94**
- Mathews, Salima et al., "Recombinant Human Renin Produced in Different Expression Systems: Biochemical Properties and 3D Structure," *Protein Expression and Purification*, 7:81-91, 1996 – **Exhibit 95**
- Matteucci, M. D. and M. H. Caruthers, "Synthesis of Deoxyoligonucleotides on a Polymer Support," *Journal of the American Chemical Society*, 103:3185-91, 1981 – **Exhibit 96**
- Miller, A. Dusty and Carol Buttimore, "Redesign of Retrovirus Packaging Cell Lines to Avoid Recombination Leading to Helper Virus Production," *Molecular and Cellular Biology*, 6:2895-902, 1986 – **Exhibit 97**

- Miyatake, S. et al., "Structure of the chromosomal gene for granulocyte-macrophage colony stimulating factor: comparison of the mouse and human genes," *EMBO Journal*, 4:2561-8, 1985 – **Exhibit 98**
- Morishita, Ryuichi et al., "Single intraluminal delivery of antisense cdc2 kinase and proliferating-cell nuclear antigen oligonucleotides results in chronic inhibition of neointimal hyperplasia," *Proceedings of the National Academy of Sciences USA*, 90:8474-8, 1993 – **Exhibit 99**
- Moss, Bernard, "Vaccinia and other poxvirus expression vectors," *Current Opinion in Biotechnology*, 3:518-22, 1992 – **Exhibit 100**
- Naviaux, Robert K. and Inder M. Verma, "Retroviral vectors for persistent expression *in vivo*," *Current Opinion in Biotechnology*, 3:540-7, 1992 – **Exhibit 101**
- Nedwin, Glenn E. et al, "Human lymphotoxin and tumor necrosis factor genes: structure, homology and chromosomal localization," *Nucleic Acids Research*, 13:6361-73, 1985 – **Exhibit 102**
- Nguyen, Geneviève et al, "Specific receptor binding of renin on human mesangial cells in culture increases plasminogen activator inhibitor-1 antigen," *Kidney International*, 50:1897-903, 1996 – **Exhibit 103**
- Noble, Nancy A. and Wayne A. Border, "Angiotensin II in Renal Fibrosis: Should TGF- $\beta$  Rather Than Blood Pressure be the Therapeutic Target?," *Seminars in Nephrology*, 17:455-66, 1997 – **Exhibit 104**
- Ohno, Minoru et al., "Fluid Shear Stress Induces Endothelial Transforming Growth Factor Beta-1 Transcription and Production," *Journal of Clinical Investigation*, 95:1363-9, 1995 – **Exhibit 105**
- Okuda, Seiya et al., "Elevated Expression of Transforming Growth Factor- $\beta$  and Proteoglycan Production in Experimental Glomerulonephritis," *Journal of Clinical Investigation*, 86:453-62, 1990 – **Exhibit 106**
- Peten, Emmanuel P. et al., "The Contribution of Increased Collagen Synthesis to Human Glomerulosclerosis: A Quantitative Analysis of  $\alpha$ 2IV Collagen mRNA Expression by

Competitive Polymerase Chain Reaction," *Journal of Experimental Medicine*, 176:1571-6, 1992 – **Exhibit 107**

- Peters, Harm et al., "Therapeutic reduction of TGF- $\beta$  and matrix proteins in Thy 1-induced glomerulonephritis is enhanced by angiotensin blockade at higher doses and further enhanced by addition of low protein diet," *Journal of the American Society of Nephrology*, 8:A2438, 1997 – **Exhibit 108**
- Peters, H. et al., "Angiotensin II Blockade Reduces Glomerular Transforming Growth Factor  $\beta$  and Matrix Protein Synthesis in Undiseased Rats," *Kidney & Blood Pressure Research*, 21:131-2, 1998 – **Exhibit 109**
- Peters, Harm et al., "Targeting TGF- $\beta$  overexpression in renal disease: Maximizing the antifibrotic action of angiotensin II blockade," *Kidney International*, 54:1570-80, 1998 – **Exhibit 110**
- Price, Jack et al., "Lineage analysis in the vertebrate nervous system by retrovirus-mediated gene transfer," *Proceedings of the National Academy of Sciences USA*, 84:156-60, 1987 – **Exhibit 111**
- Rahuel, Joseph et al., "The Crystal Structures of Recombinant Glycosylated Human Renin Alone and in Complex with a Transition State Analog Inhibitor," *Journal of Structural Biology*, 107:227-36, 1991 – **Exhibit 112**
- Rajaonarivony, M. et al., "Development of a New Drug Carrier Made from Alginate," *Journal of Pharmaceutical Sciences*, 82:912-7, 1993 – **Exhibit 113**
- Ray, Patricio E. et al., "Renal vascular induction of TGF- $\beta$ 2 and renin by potassium depletion," *Kidney International*, 44:1006-13, 1993 – **Exhibit 114**
- Ray, Patricio E. et al., "Modulation of Renin Release and Renal Vascular Smooth Muscle Cell Contractility by TGF- $\beta$ 2," *Progression of Chronic Renal Diseases*, 118:238-48, 1996 – **Exhibit 115**
- Remuzzi, Giuseppe et al., "Understanding the nature of renal disease progression," *Kidney International*, 51:2-15, 1997 – **Exhibit 116**

- Remuzzi, Giuseppe and Norberto Perico, "Protecting Single-Kidney Allografts from Long-Term Functional Deterioration," *Journal of the American Society of Nephrology*, 9:1321-32, 1998 – **Exhibit 117**
- Riser, Bruce L. et al., "Intraglomerular Pressure and Mesangial Stretching Stimulate Extracellular Matrix Formation in the Rat," *Journal of the Clinical Investigation*, 90:1932-43, 1992 – **Exhibit 118**
- Riser, Bruce L. et al., "Mesangial Cell (MC) Stretch Stimulates the Secretion and Activation of Transforming Growth Factor Beta 1 (TGF- $\beta$ 1) But Not TGF- $\beta$ 2/TGF- $\beta$ 3," *Journal of the American Society of Nephrology*, 4:67P, 1993 – **Exhibit 119**
- Rocco, Michael V. et al., "Elevated glucose stimulates TGF- $\beta$  gene expression and bioactivity in proximal tubule," *Kidney International*, 41:107-14, 1992 – **Exhibit 120**
- Rondeau, E. et al., "Plasminogen activator inhibitor 1 in renal fibrin deposits of human nephropathies," *Clinical Nephrology*, 33:55-60, 1990 – **Exhibit 121**
- Rosenberg, Mark E. et al., "Effect of Dietary Protein on Rat Renin and Angiotensinogen Gene Expression," *Journal of Clinical Investigation*, 85:1144-9, 1990 – **Exhibit 122**
- Ruiz-Ortega, M. et al., "Platelet Activating Factor (PAF) Stimulates the Expression and Synthesis of Extracellular Matrix Proteins in Cultured Renal Cells," *Journal of the American Society of Nephrology*, 5:64P, 1994 – **Exhibit 123**
- Sahai, Atul et al., "Chronic Hypoxia Stimulates the Expression of Extracellular Matrix Proteins and TGF- $\beta$  in Cultured Mesangial Cells," *Journal of the American Society of Nephrology*, 6:1877, 1995 – **Exhibit 124**
- Sealey, Jean E. et al., "Specific Prorenin / Renin Binding (ProBP): Identification and Characterization of a Novel Membrane Site," *American Journal of Hypertension*, 9:491-502, 1996 – **Exhibit 125**
- Sharma, Kumar et al., "Neutralization of TGF- $\beta$  by Anti-TGF- $\beta$  Antibody Attenuates Kidney Hypertrophy and the Enhanced Extracellular Matrix Gene Expression in STZ-Induced Diabetic Mice," *Diabetes*, 45:522-30, 1996 – **Exhibit 126**

- Shah, Mamta et al., "Control of scarring in adult wounds by neutralising antibody to transforming growth factor  $\beta$ ," *The Lancet*, 339:213-4, 1992 – **Exhibit 127**
- Sherman, Patti M. et al., "Identification of Tissue-type Plasminogen Activator-specific Plasminogen Activator Inhibitor-1 Mutants," *Journal of Biological Chemistry*, 270:9301-6, 1995 – **Exhibit 128**
- Shoemaker, Sara G. et al., "Transcriptional regulation of interleukin 3 gene expression in T lymphocytes," *Proceedings of the National Academy of Sciences USA*, 87:9650-4, 1990 – **Exhibit 129**
- Shull, Marcia M. et al., "Targeted disruption of the mouse transforming growth factor- $\beta$ 1 gene results in multifocal inflammatory disease," *Nature*, 359:693-9, 1992 – **Exhibit 130**
- Sielecki, Anita R. et al., "Structure of Recombinant Human Renin, a Target for Cardiovascular-Active Drugs, at 2.5 Å Resolution," *Science*, 243:1346-51, 1989 – **Exhibit 131**
- Smith, Theodore A. G. et al., "Adenovirus mediated expression of therapeutic plasma levels of human factor IX in mice," *Nature Genetics*, 5:397-402, 1993 – **Exhibit 132**
- Tomooka, Suguru et al., "Glomerular matrix accumulation is linked to inhibition of the plasmin protease system," *Kidney International*, 42:1462-9, 1992 – **Exhibit 133**
- Uotila, Marjatta et al., "Two-Site Sandwich Enzyme Immunoassay with Monoclonal Antibodies to Human Alpha-Fetoprotein," *Journal of Immunological Methods*, 42:11-5, 1981 – **Exhibit 134**
- Véniant, Murielle et al., "Vascular Damage without Hypertension in Transgenic Rats Expressing Prorenin Exclusively in the Liver," *Journal of Clinical Investigation*, 98:1966-70, 1996 – **Exhibit 135**
- Wagner, Richard W., "Gene inhibition using antisense oligodeoxynucleotides," *Nature*, 372:332-5, 1994 – **Exhibit 136**
- Wagner, Richard W. et al., "Antisense Gene Inhibition by Oligonucleotides Containing C-5 Propyne Pyrimidines," *Science*, 260:1510-3, 1993 – **Exhibit 137**

- Wexler, Ruth R. et al., "Rationale for the Chemical Development of Angiotensin II Receptor Antagonists," *American Journal of Hypertension*, 5:209S-20S, 1992 – **Exhibit 138**
- Yei, Soonpin et al., "Adenovirus-mediated gene transfer for cystic fibrosis: quantitative evaluation of repeated in vivo vector administration to the lung," *Gene Therapy*, 1:192-200, 1994 – **Exhibit 139**
- Yu, C. Yung et al., "Cosmid Cloning and Walking to Map Human CD1 Leukocyte Differentiation Antigen Genes," *Methods of Enzymology*, 217:378-98, 1993 – **Exhibit 140**
- Zhu, Ning et al., "Systemic Gene Expression After Intravenous DNA Delivery into Adult Mice," *Science*, 261:209-11, 1993 – **Exhibit 141**
- Ziyadeh, Fuad N. et al., "Stimulation of Collagen Gene Expression and Protein Synthesis in Murine Mesangial Cells by High Glucose is Mediated by Autocrine Activation of Transforming Growth Factor- $\beta$ ," *Journal of Clinical Investigation*, 93:536-42, 1994 – **Exhibit 142**

This statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(a)(2), copies of each document or other information listed on the enclosed Form 1449 are provided.

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that the references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. § 609, it is requested that the Examiner return a copy of the attached Form 1449,

marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,

Sarah B. Adriano

Sarah B. Adriano  
Registration No. 34,470  
SaraLynn Mandel  
Registration No. 31,853  
Attorneys for Applicants  
Mandel & Adriano  
35 No. Arroyo Parkway, Suite 60  
Pasadena, California 91103  
(626) 395-7801  
Customer No. 26,941